Claim 1 is objected to because of a minor informality. Additionally, the status of claim 6 is said to be unclear. In response, the informality has been addressed in amended claim 1. Additionally, by the above direction to cancel claim 6, the status thereof is made abundantly clear. Accordingly, these matters are mooted.

Claims 1, 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the reasons noted. By the above amendment to claims 1, 4, 5, 18 and 19, and cancellation of claims 2 and 7, this rejection is overcome.[1/]

Claims 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification as filed. By the above amendment to claims 4, 5, 7, 18 and 19 and cancellation of claim 2, this rejections is overcome.

Claims 1, 2, 4, 5 and 7 are rejected under 35 U.S.C. §112, first paragraph, because the specification is said not to reasonably enable making and using all isolated DNAs hybridizing with said SEQ ID NOs or comprising a nucleotide sequence identical to any continuous 10 to 50 residues therefrom. This rejection respectfully traversed.

In response, Applicants respectfully submit that since the claimed oligonucleotides are constituted by DNA, it was well-known and apparent for one of ordinary skill in the art (at the filing of the present application) that oligo DNA could

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1/ In this regard, the Examiner further asserts it is unclear whether claim 4 is directed to detection of any specific mRNA. Therefore, in amended claims 4 and added 20, the mRNA is limited to a mRNA whose expression level increases in leukocytes of IgA nephropathy patients. As shown at page 46, Table 1 and page 67, lines 3-10, the expression level of the mRNA measured by this process increases in leukocytes of IgA nephropathy patients.

readily be produced by a DNA synthesizer. *See* specification page 15, lines 21-25. With regard to application of the oligonucleotides, such can be used as a primer in diagnosis of IgA nephropathy by PCR, and that the antisense oligonucleotide can be used for treatment of IgA nephropathy. *See* from page 33, line 19 to page 34, line 21.

The Examiner further asserts that any given 100-1000 base pair sequence would be expected to contain multiple matches to unrelated nucleotide sequences containing at least 10 continuous residues. Among the sequences noted by the Examiner, the sequences in Hiller (GenBank H71225), Bader (GenBank U23946), Hiller (GenBank N89899) and Hiller (GenBank T98890) are EST of the DNA of the present invention (or cDNA of which splicing is different), and therefore relate to IgA nephropathy. Also, the sequences in Hettmann (GenBank S71037), Kelly (GenBank X02228) and Trick (GenBank X52089) are not exon, and therefore do not transfer to mRNA. Accordingly, they cannot be detected by the detection method of the present invention.

Of the sequences cited by the Examiner, sequences which are unrelated to IgA nephropathy but are detected by the detection method of the present invention would be the sequence of Hiller (GenBank H73595) containing 17 bp sequence which is identical with a part of the sequence of SEQ ID NO:9 and Hudson (GenBank G24450) containing 17 bp sequence which is identical with a part of the sequence of SEQ ID NO:11.

Among 1000 bp sequence, 991 kinds are present as continuous 10 bp sequences. Accordingly, the probability where one 10 bp sequence selected as a probe is continuously present in the 1000 bp sequence is $991/410 = 991/1048576 = 0.000945$. Thus, the probability where sequences unrelated to IgA nephropathy are detected is very

low, but is not zero. Therefore, there are accidental coincidences with regard to SEQ ID NO:9 and 11. Thus, claim 4 is now better directed to a method of detecting mRNA using one probe, wherein probes having accidentally coincident sequences relating to SEQ ID NO:9 and 11 are deleted from the claim, and the DNA is limited to a DNA comprising a nucleotide sequence identical to any continuous 10 to 50 residues in a nucleotide sequence selected from the nucleotide sequences consisting of complementary sequences of SEQ ID NO:1-6.

With regard to new claim 22, when a mRNA is detected by PCR using a sense primer and an antisense primer as disclosed at page 33, line 19 to page 34, line 10 and page 43, line 9 to page 48, line 4 (Example 2) in the specification, it is necessary that there are two sequences of 10 bp or more which are continuously identical with respective primer sequences (complementary sequence in the antisense primer) and that the lengths of the amplified fragment are also identical. Therefore, mRNA unrelated to IgA nephropathy would not be amplified in the same manner as mRNA in the sequences of SEQ ID NO:1-6 and 9-12. Accordingly, in claim 22 (and amended claim 5), the sequences of SEQ ID NO:1-6 and 9-12 in which expression of mRNA level increases due to IgA nephropathy are distinguished from other sequences by using a DNA comprising 10 to 50 residues in a nucleotide sequence selected from the nucleotide sequences consisting of SEQ ID NO:1-6 and 9-12 (sense primer) and a DNA comprising a nucleotide sequence identical to any continuous 10 to 50 residues in a nucleotide sequence selected from the nucleotide sequences consisting of complementary sequences of SEQ ID NO:1-6 and 9-12 (antisense primer).

Claim 7 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art. This rejection is mooted by the cancellation of this claim.

Claims 1, 2 and 5 are rejected under 35 U.S.C. §102(b) as being clearly anticipated by:

Name	GenBank Accession No.	Date
Hillier	H71225	10/26/95
Bader	U23946	5/16/96
Hettmann	S71037	9/23/94
Kelly	X02228	4/24/93
Hillier	B89899	4/02/96
Hillier	H73595	10/31/95
Trick	X52089	3/23/95
Hudson	G24450	5/31/96
Hillier	T98890	3/31/95

Additionally, Claims 18 and 19 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Hillier (GenBank Accession No. H71225, 10/26/95), Bader (GenBank Accession No. U23946, 5/16/96), Hettmann (GenBank Accession No. S71037, 9/23/94), Kelly (GenBank Accession No. X02228, 4/24/93), Hillier (GenBank Accession No. B89899, 4/02/96), Hillier (GenBank Accession No. H73595, 10/31/95), Trick (GenBank Accession No. X52089, 3/23/95), Hudson (GenBank Accession No. G24450, 5/31/96), Hillier (GenBank Accession No. T98890, 3/31/95).

As a result of the amendment of claim 1, the DNAs in the references cited by the Examiner are excluded from the scope of the DNA which comprises a nucleotide sequence having an identity of 60% or more with a nucleotide sequence selected from the group of nucleotide sequences consisting of SEQ ID NO:1-6 or having an identity of 95%

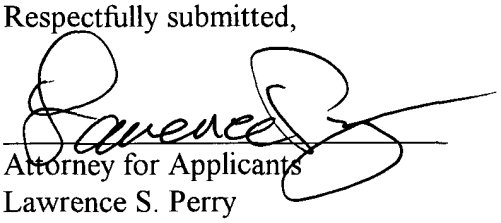
or more with a nucleotide sequence selected from the group of nucleotide sequences consisting of SEQ ID NO:9-12 as defined in amended claim 1. Additionally, with regard to claim 5, the references cited by the Examiner do not disclose use of the DNA for diagnosis of IgA nephropathy and a diagnostic agent for IgA nephropathy using the DNA.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1, 4, 5, 18, 19 and 22 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO CLAIMS

1. (Twice Amended) An isolated DNA comprising a nucleotide sequence selected from the group of nucleotide sequences consisting of SEQ ID NO:1-6 and 9-12, or a DNA which [hybridizes with said DNA at 65°C in the presence of 0.7-1.0M NaCl using a filter on which said DNA is immobollized followed by washing the filter with 0.1 ′ to 2 ′ SSC solution (where 1 ′ SSC is 150 mM sodium chloride and 15 mM sodium citrate) at 65°C] comprises a nucleotide sequence having an identity of 60% or more with a nucleotide sequence selected from the group of nucleotide sequences consisting of SEQ ID NO:1-6 or having an identity of 95% or more with a nucleotide sequence selected from the group of nucleotide sequences consisting of SEQ ID NO:9-12.

Claim 2 (Cancelled)

4. (Twice Amended) A method for detecting a mRNA [using the DNA according to any one of claims 1 or 2] whose expression level increases in leukocytes of IgA nephropathy patients as compared with those of healthy persons by Northern hybridization, comprising:

(a) isolating a total RNA from a sample;

(b) hybridizing with the DNA according to claim 1 or a DNA comprising a nucleotide sequence identical to any continuous 10 to 50 residues in a

nucleotide sequence selected from the nucleotide sequences consisting of complementary sequences of SEQ ID NO:1-6 as a probe; and

(d) detecting the mRNA hybridized with the probe.

5. (Twice Amended) An IgA nephropathy diagnostic agent comprising the DNA according to [any one of] claim[s] 1 or [2] DNA comprising a nucleotide sequence identical to any continuous 10 to 50 residues in a nucleotide sequence selected from the nucleotide sequences consisting of SEQ ID NO:1-6 and 9-12 and complementary sequences to SEQ ID NO:1-6 and 9-12.

Claim 6 (Cancelled).

Claim 7 (Cancelled).

18. (Twice Amended) A composition comprising the DNA according to [any one of] claim[s] 1 [or 2] and a diagnostic acceptable carrier.

19. (Twice Amended) A composition comprising the DNA according to claim [2] 1 and a pharmaceutical acceptable carrier.